Applicants' attorney and Andre Bourgouin, the patent counsel for the Assignee of the present application, wish to thank the Examiner in charge of the application for the courtesies extended to them at the interview on July 10, 2002 at which time, the rejection of January 30, 2002 was discussed.

The present amendment corrects claim 24 by deleting the term "analog" therefrom and therefore, this is now drawn to allowable subject matter. Claim 18 and the claims dependent thereon have been rejected as being indefinite in the structural formula since, in the Examiner's opinion, there were dangling valences.

Applicants respectfully traverse this ground of rejection since the amended claims are believed to properly define the invention and the novelty of Applicants' invention resides in the fact that they are drawn to a substituted or unsubstituted camptothecin with a 7-ring member ß-hydroxy lactone ring and this can be clearly seen from the structural formula in claim 18 at the present time. As pointed out on pages 1 and 2 of the application as filed, the novel compounds differ from all known derivatives of camptothecin in that they contain the ß-hydroxy lactone instead of an α-hydroxy lactone and its pharmaceutical salts. Apart from this, the compounds can have the same structural skeleton as that of the known camptothecins with or without other chemical substitutions on the skeletal structure which are well known to those skilled in the art. Applicants have already tested 137

compounds as can be seen from the Thurieau declaration and all have activity.

As pointed out to the Examiner at the interview, the novelty resides in the fact that the 7-membered ring ß-lactones are active for treating cancers which was completely surprising for those skilled in the art. In the preliminary amendment dated July 7, 2000 filed with the application, there were three publications submitted and the Examiner's attention is directed to the same and this would lead one skilled in the art away from using a 7-ring member ß-hydroxy lactone for the treatment of cancer. The Examiner's attention is directed thereto. Even after publication of Applicants' initial disclosure with respect to the novel compounds, there were publications indicating that those skilled in the art were completely surprised that the 7-ring member ß-hydroxy lactone ring compounds were active. Applicants are submitting herewith a declaration by Christope Thurieau which reports on the testing of 137 compounds falling within the scope of the above application and all of them were useful for the treating of various cancers. The cancers tested included cancer of the bladder, the breast, the central nervous system, the colon, leukemia, lung and prostate and all the compounds were active against the various cancers, obviously varying in degree depending upon the specific compound. However, they were all active and this is completely surprising. It is deemed that Applicants have clearly demonstrated that the claimed compounds are unexpectedly suitable for the

treatment of the various cancers and that the claims are of sufficient scope and are clearly supported by the specification as filed. Therefore, withdrawal of this ground of rejection is requested.

In view of the amendments to the claims and the above remarks, it is believed that the claims clearly point out Applicants' patentable contribution and favorable reconsideration of the application is requested.

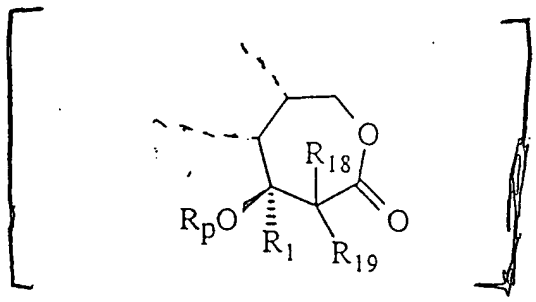
Respectfully submitted,
Bierman, Muserlian and Lucas

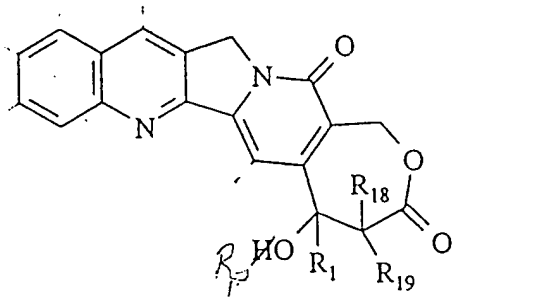
By: 
Charles A. Muserlian #19,683
Attorney for Applicants
Tel.# (212) 661-8000

CAM:ds
Enclosures

MARKED UP VERSION OF CLAIMS SHOWING CHANGES MADE

Claim 18 (thrice amended) A method of treating a cancer selected from the group consisting of leukemia, colon cancer, lung cancer, prostate cancer and breast cancer in warm-blooded animals comprising administering to warm-blooded animals in need thereof a unsubstituted or substituted camptothecin analog with a 7-ring member ß-hydroxy lactone ring of the formula





wherein R_1 is selected from the group consisting of alkyl of 1 to 6 carbon atoms, alkenyl and alkynyl of 2 to 6 carbon atoms haloalkyl of 1 to 6 carbon atoms, alkoxy alkyl of 2 to 12 carbon atoms and alkylthioalkyl of 2 to 12 carbon atoms, R_p is hydrogen or an easily cleavable group, R_{18} and R_{19} are individually selected from the group consisting of hydrogen, halogen, OH and alkyl and alkoxy of 1 to 6 carbon atoms and its non-toxic, pharmaceutically acceptable salts.

Claim 24 (amended) The method of claim 18 wherein the camptothecin [analog] is (+)-5-ethyl-9,10-difluoro-5-hydroxy-4,5,13,15-tetrahydro-1H,3H-oxepino[3',4':6,7] indolizino[1,2-b] quinoline-3,15-dione or (+)-1-[9-chloro-5-ethyl-5-hydroxy-10-methyl-3,15-dioxo-4,5,13,15-tetrahydro-1H,3H-oxpino[3',3':6,7]indolizino[1,2-b]quinolin-12-ylmethyl]-4-methyl-hexahydropyridium chloride.